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EXAMINER

18N1/1211

ART UNIT	PAPER NUMBER
1807	14

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DATE MAILED: 12/11/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 3-30-95 ☑ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ——— days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-29 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☑ Claims 30-35 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-29 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. Applicant's response, filed 3/30/95, has been carefully considered with the following effect:

The objection and rejections of paragraphs 16, 17A, 17B, Office action mailed 12/30/94, have been withdrawn in view of applicant's arguments and amendments to the claims.

The objections and rejections of paragraphs 18, 19, 21, 23 and 24, Office action mailed 12/30/94, have been maintained.

16. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

17. The specification is objected to under 35 U.S.C. § 112, first paragraph, for failing to adequately teach how to use the invention, i.e. failing to provide an enabling disclosure.

18. Claims 1-29 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

19. Applicant argues that the specification teaches that there are several uses for the claimed compounds that do not involve hybridization, for example, improved transport across cellular membranes, intercalators, nucleic acid cleaving agents and cell surface phospholipids.

These arguments are not persuasive. The specification does not provide any guidance as to how the various utilities are

enabled without some DNA hybridization activity. For example, there is no guidance as to how a compound merely with "improved transport across cellular membranes" or a compound that functions as a "cell surface phospholipid" but without the ability to bind to DNA, is to be used.

The other uses, nucleic acid intercalators and nucleic acid cleaving agents must have some affinity to DNA in order to function.

Also, assuming that there is some utility for the properties of "improved transport across cellular membranes" or "cell surface phospholipid," the claims still read on a broad variety of compounds and a large fraction of the compounds will not have these properties for the reasons given in the last Office action with respect to the nucleic acid hybridization ~~assay~~ activity.

For example, the scope of the claimed substituent "R_A-$N(R_{1a})(R_{1b})$" ranges from:

" $-CH_2-NH_2$ "

to:

" $[CH_2-CH_2-Q-)_{200}]N[(C(X)-Q-(CH_2-CH_2-Q-)_{200} - (CH_2-CH_2-Q-)_{200} - CH_2-CH_2-Q-)_{200} - NH_2][(C(X)-Q-(CH_2-CH_2-Q-)_{200} - (CH_2-CH_2-Q-)_{200} - (CH_2-CH_2-Q-)_{200} - NH_2]$ "

In the above case, the following values were given for the various side groups:

$R_A = (CH_2-CH_2-Q)_x$, and x = 200, (R_{1a}) and $(R_{1b}) = C(X)-Q-R_A-R_2$; $R_2 = CH_2-CH_2-Q-)_x-R_3$; R3 = R_A-NH_2

Furthermore, the scope of the claims includes:

" containing a steroid molecule or a protein "

SH Thus, the claim encompasses compounds having 6 ~~ations~~ atoms such as " $-CH_2-NH_2$ " to an extremely large side group with over 4200 atoms. Clearly a compound containing a plurality of linked nucleosides in which each nucleoside includes a 4200 atom substituent at, say, the 3'-O-position, will be much too large to interact with a nucleic acid or to be transported across a cell membrane or any of the other stated utilities. Not only will the base to base distance will be far too great for hybridization, but also the shear bulk of the substituent will keep the compound from being transported accross a cell membrane.

The specification lacks specific guidance as to which of the myriad of side group structures between the simple " $-CH_2-NH_2$ " structure and the 4200 atom structure, will function in these utilities. Lacking this guidance, it would require undue experimentation of constructing and testing these compounds by brute force trial and error.

Applicant correctly points out that there is no requirement that all claimed compounds possess the same degree of utility. However, this argument is not persuasive because (1) clearly many of the claimed embodiments have no utility and (2) there is no guidance as to which compounds have utility and which do not.

20. Claims 1-4, 6-18 and 20-29 are rejected under 35 U.S.C. § 102(b) as being anticipated by Matteucci et al. WO 92/05186 4/1/92 (Matteucci).

21. Applicant argues that Matteucci is drawn to internucleosidic linkages while the claims are limited to "R_A-$N(R_{1a})(R_{1b})$" containing substituents which allegedly cannot serve as an internucleoside linkage. This argument is not persuasive. The claims recite "a plurality of linked nucleosides", substituents at 3' O-position the 5' O position.

Matteucci discloses on page 25, line 35, for example, "The positions of these atoms in the linkage can vary from the "5'" end, to the "middle" to the "3'" end." Matteucci does on to discuss specific molecules within these generic classes.

22. Claims 1-4, 6-18 and 20-29 are rejected under 35 U.S.C. § 103 as being unpatentable over Matteucci. In addition to embodiments that are anticipated by Matteucci, these claims also contain embodiments that are obvious over Matteucci. For example, these claims differ from Matteucci in the recitation of "a reporter enzyme." However, Matteucci teaches detection of base complementarity "which is then detected by conventional means. . . . radioactive, fluorescent, or chromogenic labels (Matteucci p. 24, lines 16-24)." It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use "a reporter enzyme" in place of the

prior art teaching view of "radioactive, fluorescent, or chromogenic labels" because the claimed enzyme and the prior art materials are art recognized alternative detectable labels.

23. Applicant argues on the same grounds as above. These arguments are not persuasive for the reasons given above.

24. Claims 5 and 19 are rejected under 35 U.S.C. § 103 as being unpatentable over Matteucci as applied to claim above, and further in view of applicants admissions.

25. Applicant argues on the same grounds as above. These arguments are not persuasive for the reasons given above.

26. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

27. This application is subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, since this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under

37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a first submission and the appropriate fee of $730 for a large entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

If applicant has filed multiple proposed amendments which, when entered, would conflict with one another, specific instructions for entry or non-entry of each such amendment should be provided upon payment of any fee under 37 CFR 1.17(r).

28. Papers relating to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Art Unit 1807. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Art Unit 1807 Fax number is (703) 305-7939.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 308-3885. The examiner can normally be reached on Tuesday-Friday from 8:30 AM - 6:00 PM. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott Houtteman
December 5, 1995

W. GARY JONES
SUPERVISORY PATENT EXAMINER
GROUP 1800

12/6/95